Access	DR#	•	

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's full Name: Devesh K	<u> </u>	7931 Date:	8/13/2002
Art Unit: 1623 Phone Num	nber <u>605-1199</u> S	Serial Number: 09	9/892,636
Mail Box: CM1-8B19 and Bldg/Room Loc MAIL			
If more than one search is submit	ted, please prioritize	searches in ord	er of need.
Please provide a detailed statement of the sea search Include the elected species or structure the concept or utility of the invention. Define citations, authors, etc, if known. Please attack	es, key words, synonyms, a e any terms that may have a	cronyms, and registry special meaning. Gi	numbers, and combine with ve examples or relevant
Title of Invention: See Bib Data She	eet		
Inventors (please provide full names): Se	e Bib Data Sheet	•	
Earliest priority Filing Date: See Bil	Data Sheet		
For Sequence Searches Only Please include numbers) along with the appropriate serial n		(parent, child, divisio	onal, or issued patent
Please carry out a search for	the method of treating	g lung disease in	claims 13,14,24,26,29
and 33. A copy of the claims is prov	vided.		
			* .
The Bib Data Sheet which di	iscloses the inventor r	names, title of the	invention, and the
earliest priority filing date is also pro			
· · · · · · · · · · · · · · · · · · ·			
			Point of Contact: Toby Port Technical Info. Specialist CM1 6A04 703-308-3534
	•		•
******	******	******	******
STAFF USE ONLY	Type of Search	Vendors and cost	where applicable
Searcher:	NA Sequence (#)	STN	305
Searcher Phone #:	AA Sequence (#)	Dialog	
Searcher Location:	Structure (#)	Questel/Orbit	
Date Searcher Picked Up: 91	Bibliographic	Dr. Link	
Date Completed: 9//7	Litigation	Lexis/Nexis	
Searcher Prep & Review Time: 20	Fulltext	Sequence Systems	
Clerical prep time:	Patent Family	WWW/Internet	
Online Time: 95	Other	Other (specify)	

PTO-1590 (1-2000)

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=> file reg

(FILE 'REGISTRY' ENTERED AT 15:32:21 ON 17 SEP 2002

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 SEP 2002 HIGHEST RN 452049-48-8

DICTIONARY FILE UPDATES: 16 SEP 2002 HIGHEST RN 452049-48-8
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TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d rn cn 12

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ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS 0004-54-0 REGISTRY
Dexecon (9CI) (CA INDEX NAME)
L2
RN
CN
OTHER CA INDEX NAMES:
     Dextrans (8CI)
CN
OTHER NAMES:
     .alpha.-Dextran
CN
CN
     58: PN: WO0185782 FIGURE: 18 claimed sequence
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     DEX 500
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CN
     Dextran 1.5
CN
     Dextran 10
CN
     Dextran 1000
CN
     Dextran 110
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     Dextran T 110
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     Dextran T 150
CN
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CN
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     Expandex
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     Gentran
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     Hemodex
CN
     Hyscon
CN
     Hyskon
CN
     Infucoll
CN
     Intrader
CN
     Intradex
CN
     LMD
CN
     LMWD
     Longasteril 70
CN
CN
     LU 122
     LVD
CN
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ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY

=> file hcaplus; d que 115; d que 116; d que 117; d que 124; d que 129; d que 132 FILE HCAPLUS' ENTERED AT 16:45:24 ON 17 SEP 2002 USÉ IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 17 Sep 2002 VOL 137 ISS 12 FILE LAST UPDATED: 16 Sep 2002 (20020916/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

L3	927	SEA	FILE=REGISTRY	ABB=ON	PLU=ON	9004-54-0/CRN
L4	4953	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L3
L5	30141	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	DEXTRAN
L7	87267	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	LUNG/CW

Page 3

```
L8
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                                                BRONCHI/CT
              O SEA FILE=HCAPLUS ABB=ON PLU=ON
L9
                                                BRONCHIOLE/CT
L10
           4916 SEA FILE=HCAPLUS ABB=ON
                                       PLU=ON
                                               CYSTIC FIBROSIS/CT
L11
           3338 SEA FILE=HCAPLUS ABB=ON
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                                                MUCUS/CT
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115
                L9 OR L10) AND L11
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L4
           4953 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
L5
          30141 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                DEXTRAN
          87267 SEA FILE=HCAPLUS ABB=ON PLU=ON
L7
                                                LUNG/CW
\Gamma8
          11222 SEA FILE=HCAPLUS ABB=ON PLU=ON BRONCHI/CT
L9
              O SEA FILE=HCAPLUS ABB=ON PLU=ON BRONCHIOLE/CT
L10
           4916 SEA FILE=HCAPLUS ABB=ON
                                       PLU=ON CYSTIC FIBROSIS/CT
L12
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L16
                L9 OR L10) AND L12
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           4953 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
L4
L5
          30141 SEA FILE=HCAPLUS ABB=ON PLU=ON DEXTRAN
          87267 SEA FILE=HCAPLUS ABB=ON PLU=ON LUNG/CW
L7
L8
          11222 SEA FILE=HCAPLUS ABB=ON PLU=ON BRONCHI/CT
L9
              O SEA FILE=HCAPLUS ABB=ON PLU=ON BRONCHIOLE/CT
L10
           4916 SEA FILE=HCAPLUS ABB=ON
                                       PLU=ON CYSTIC FIBROSIS/CT
            607 SEA FILE=HCAPLUS ABB=ON PLU=ON EXPECTORANTS/CT
L13_
                                       PLU=ON (L4 OR L5) AND (L7 OR L8 OR
             3 SEA FILE=HCAPLUS ABB=ON
117
              365392 SEA FILE=HCAPLUS ABB=ON PLU=ON POLYSACCHARIDES+NT/CT
L6
T.7
          87267 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                LUNG/CW
T.8
          11222 SEA FILE=HCAPLUS ABB=ON
                                        PLU=ON
                                                BRONCHI/CT
L9
              O SEA FILE=HCAPLUS ABB=ON
                                        PLU=ON
                                                BRONCHIOLE/CT
           4916 SEA FILE=HCAPLUS ABB=ON
                                        PLU=ON
                                                CYSTIC FIBROSIS/CT
T.10
                                       PLU=ON
           3338 SEA FILE=HCAPLUS ABB=ON
                                                MUCUS/CT
T.11
            (11 SEA FILE=HCAPLUS ABB=ON PLU=ON
                                                L6 AND (L7 OR L8 OR L9 OR
3L24
            L10) AND L11 AND PHARMAC?/SC,SX
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L6
                                        PLU=ON
                                                POLYSACCHARIDES+NT/CT
L7
          87267 SEA FILE=HCAPLUS ABB=ON
                                        PLU=ON
                                                LUNG/CW
L8
          11222 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                BRONCHI/CT
L9
              O SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                BRONCHIOLE/CT
                                         PLU=ON
                                                CYSTIC FIBROSIS/CT
L10
           4916 SEA FILE=HCAPLUS ABB=ON
                                         PLU=ON
                                                EXPECTORANTS/CT
L13
            607 SEA FILE=HCAPLUS ABB=ON
L27
                                        PLU=ON
                                                L6 AND (L7 OR L8 OR L9 OR
             13 SEA FILE=HCAPLUS ABB=ON
                _L10) AND L13
            11 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 NOT (GENES OR INFECTION?
            / OR MATRIX)/TI
L3
            927 SEA FILE=REGISTRY ABB=ON PLU=ON 9004-54-0/CRN
T.4
           4953 SEA FILE=HCAPLUS ABB=ON PLU=ON L3
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L5
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                                          PLU=ON DEXTRAN
L7
          87267 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                 LUNG/CW
1.8
          11222 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  BRONCHI/CT
L9
               O SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  BRONCHIOLE/CT
           4916 SEA FILE=HCAPLUS ABB=ON
L10
                                          PLU=ON
                                                  CYSTIC FIBROSIS/CT
L30
          19846 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  MUCIN? OR MUCOUS?
L31
               5 SEA FILE=HCAPLUS ABB=ON
                                          PLU=ON
                                                  (L4 OR L5) AND (L7 OR L8 OR
                L9 OR L10) AND L30
L32
              M SEA FILE-HCAPLUS ABB-ON
                                          PLU=ON L31 AND DOGS/TI
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=> \$ 115 or 117 or 124 or 129 or 132 176 20 L15 OR L17 OR L24 OR L29 OR L32

=> file medline; d que 149 FILE 'MEDLINE' ENTERED AT 16:46:05 ON 17 SEP 2002

FILE LAST UPDATED: 14 SEP 2002 (20020914/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2002 vocabulary. Enter HELP THESAURUS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

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L33
        256083 SEA FILE=MEDLINE ABB=ON PLU=ON POLYSACCHARIDES+NT/CT
         371931 SEA FILE=MEDLINE ABB=ON PLU=ON LUNG DISEASES+NT/CT
L34
L35
           5738 SEA FILE=MEDLINE ABB=ON
                                        PLU=ON
                                                MUCUS/CT
L45
         122792 SEA FILE=MEDLINE ABB=ON
                                        PLU=ON
                                                L33/MAJ
L46
         283437 SEA FILE=MEDLINE ABB=ON
                                        PLU=ON
                                                L34/MAJ
            [ 1 SEA FILE=MEDLINE ABB=ON PLU=ON L45 AND L46 AND (L35 (L)
L49 ¥
             DE/CT OR MUCOCILIARY CLEARANCE/CT)
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=> file_embase; d que 158 FTLE 'EMBASE' ENTERED AT 16:46:11 ON 17 SEP 2002 COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

FILE COVERS 1974 TO 13 Sep 2002 (20020913/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

L50	70742	SEA	FILE=EMBASE	ABB=ON	PLU=ON	POLYSACCHARIDE+NT/CT
L51	236280	SEA	FILE=EMBASE	ABB=ON	PLU=ON	LUNG DISEASE+NT/CT
L52	15972	SEA	FILE=EMBASE	ABB=ON	PLU=ON	CYSTIC FIBROSIS/CT
L53	41394	SEA	FILE=EMBASE	ABB=ON	PLU=ON	BRONCHUS DISEASE+NT/CT
L54	1988	SEA	FILE=EMBASE	ABB=ON	PLU=ON	MUCUS/CT
L55	748	SEA	FILE=EMBASE	ABB=ON	PLU=ON	BRONCHUS MUCUS/CT
L56	1343	SEA	FILE=EMBASE	ABB=ON	PLU=ON	MUCOCILIARY CLEARANCE/CT
L57	6	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L50 AND (L51 OR L52 OR L53)
		_ĄŅD				
L58	(\$5	SEA	FILE=EMBASE	ABB=ON	PLU=ON	L57 NOT LUNG CANCER/CT

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=> file_biosis; d que 165

FILE 'BIOSIS' ENTERED AT 16:47:36 ON 17 SEP 2002

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FILE COVERS 1969 TO DATE. CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 11 September 2002 (20020911/ED)

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13 927 SEA FILE=REGISTRY ABB=ON PLU=ON 9004-54-0/CRN
159 50285 SEA FILE=BIOSIS ABB=ON PLU=ON L3 OR DEXTRAN OR POLYSACCHARIDE
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160 350912 SEA FILE=BIOSIS ABB=ON PLU=ON LUNG OR CYSTIC FIBROSIS OR
161 BRONCH?
161 25516 SEA FILE=BIOSIS ABB=ON PLU=ON MUCUS? OR MUCOUS? OR MUCOCILIAR
17 SEA FILE=BIOSIS ABB=ON PLU=ON L59 AND L60 AND L61
1855 ABB=ON PLU=ON L64 AND DEXTRAN/TI
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=> file wpid; d que 175

FILE WPIDS ENTERED AT 16:47:45 ON 17 SEP 2002

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FILE LAST UPDATED: 16 SEP 2002 <20020916/UP>
MOST RECENT DERWENT UPDATE 200259 <200259/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

- >>> The BATCH option for structure searches has been
 enabled in WPINDEX/WPIDS and WPIX >>>
- >>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY >>>
- >>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
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 PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<</pre>
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 GUIDES, PLEASE VISIT:
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L66
           4407 SEA FILE=WPIDS ABB=ON
                                        PLU=ON
                                                DEXTRAN
L67
          14916 SEA FILE=WPIDS ABB=ON
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                                        PLU=ON
                                                LUNG
L68
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                                                CYSTIC FIBROSIS
           2086 SEA FILE=WPIDS ABB=ON
                                        PLU=ON
L69
          10270 SEA FILE=WPIDS ABB=ON
                                        PLU=ON
                                                BRONCH?
L70
L71
           1659 SEA FILE=WPIDS ABB=ON
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L72
                MUCOCILIAR?
                                        PLU=ON (L66 OR L67) AND (L68 OR L69 OR
L74
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                L70 OR L71) AND L72
             SEA FILE-WPIDS ABB-ON PLU-ON L74 AND (DEXTR? OR MONOMER OR
10075
                ADHESION OR MUCOLYTIC)/TI
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=> dup rem 149 176 175 158 165
FILE 'MEDLINE' ENTERED AT 16:48:30 ON 17 SEP 2002
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PROCESSING COMPLETED FOR L58 PROCESSING COMPLETED FOR L65

[32 DUP REM L49 L76 L75 L58 L65 (5 DUPLICATES REMOVED) ANSWER '1' FROM FILE MEDITINE'
ANSWERS '2-21" FROM FILE MEDITION
ANSWERS 22-26 FROM FILE WELDS
ANSWERS 27-30 FROM FILE EMBASE
ANSWERS 31-32' FROM FILE BIOSIS

= 3 d ibib ab 177 1-32

L77 ANSWER 1 OF 32 MEDLINE

DUPLICATE 4

ACCESSION NUMBER:

1998176757

98176757 PubMed ID: 9517580 DOCUMENT NUMBER:

TITLE:

Improved clearability of cystic fibrosis sputum with

dextran treatment in vitro

Feng-W; -Garrett-H; Speert-D-P; King M AUTHOR:

CORPORATE SOURCE:

Pulmonary Research Group, University of Alberta, Edmonton, Canada.

MEDLINE

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE, SOURCE:

(1998 Mar) 157 (3 Pt 1) 710-4. Journal code: 9421642. ISSN: 1073-449X.

PUB. COUNTRY: United States

Journal; Article; (JOURNAL ARTICLE) DOCUMENT TYPE:

LANGUAGE: English

Abridged Index Medicus Journals; Priority Journals FILE SEGMENT:

199804 ENTRY MONTH:

Entered STN: 19980416 ENTRY DATE:

Last Updated on STN: 19980416 Entered Medline: 19980407

Most patients with cystic fibrosis (CF) are infected by Pseudomonas AR aeruginosa. Dextran exhibits anti-adhesive effects in preventing attachment of P. aeruginosa to epithelial cells (1). The initial purpose of this study was to evaluate the potential of dextran to alter the rheology and ciliary transportability of CF sputum prior to initiation of a clinical trial in patients with CF. Sputum samples were collected from 25 patients with CF not receiving rhDNase therapy for use in in vitro testing. Aliquots of CF sputum were treated with 10% vol. Ringer's or the same volume of Dextran 4000 to give a final concentration of 0.4% (4 mg/ml) or 4% (40 mg/ml) dextran in the sputum. Dog mucus samples were collected from seven healthy, anesthetized dogs from the endotracheal tube

cuff. Aliquots of dog mucus were subjected to the same concentrations of dextran as the CF sputum. All treated samples were incubated for 30 min at 37 degrees C, and their rheologic properties (viscoelasticity) were evaluated by magnetic microrheometry. For 17 of the sputum samples, frog palate mucociliary transportability was determined from sputum movement on the ciliated, mucus-depleted frog palate, relative to native frog mucus control. Spinnability (cohesiveness) was evaluated by the filancemeter technique for eight sputum samples. Overall, whether for CF sputum or healthy dog mucus, Dextran 4000 treatment significantly reduced viscoelasticity and increased predicted mucociliary and cough clearability. Direct measurements of sputum mucociliary clearability on frog palate increased significantly with 0.4% dextran and 4% dextran compared with saline control. Sputum spinnability (cohesiveness) decreased significantly with both dextran concentrations, too. The effects on viscoelasticity and spinnability were greater at 4% than at 0.4%. There was a significant positive correlation between spinnability and viscoelasticity, and negative relationships between spinnability and both forms of clearability as predicted from viscoelastic measurements. This study suggests that treatment with Dextran 4000 can reduce the crosslink density and cohesiveness of CF and improve mucociliary and cough clearability. Dextran 4000 is an inexpensive and nontoxic agent that may be of benefit in patients with CF lung disease and perhaps in other respiratory disease where mucus retention is an important feature.

```
L77 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2002 ACS
                                                      DUPLICATE 1
                        2001:167786 HCAPLUS
ACCESSION NUMBER:
                        134:212736
DOCUMENT NUMBER:
TITLE:
                        [Pharmaceutical compositions of charged dextran?
                        as a mucoactive agent for treatment of respiratory
                        disorders
                        King, Malcolm
INVENTOR(S):
                        Governors of the University of Alberta, Can.
PATENT ASSIGNEE(S):
                        PCT Int. Appl., 29 pp.
SOURCE:
                        CODEN: PIXXD2
DOCUMENT TYPE:
                        Patent
LANGUAGE:
                        English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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APPLICATION NO.
     PATENT NO.
                 KIND DATE
                     A2
                                                           (20000825----
     WO 2001015672
                            20010308
                                          WO 2000-CA989
     WO 2001015672
                     A3
                            20020228
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             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                          EP 2000-954242 20000825
                           20020612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: US 1999-150605P P 19990826
                                                        W 20000825
                                        WO 2000-CA989
```

AB The present invention is for a charged dextran, preferably dextran sulfate, as an improved mucoactive agent which can be used to improve viscoelasticity and clearance of respiratory tract mucus. The charged dextran can be used in the treatment of animals with

impaired mucus clearance, mucus retention and/or mucus hypersecretion, such as cystic fibrosis, chronic bronchitis, bronchiectasis, bronchiolitis and bronchial asthma. Related methods of treatment and pharmaceutical compns., particularly aerosolized dextran sulfate compns. are encompassed within the scope of the invention. For example, delivery of aerosolized dextran sulfate to canine airways led to reduced viscoelasticity in improved clearability of the tracheal mucus.

L77 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER: 1999:48630 HCAPLUS

DOCUMENT NUMBER: 130:76186

TITLE: Use of dextran and other polysaccharides to

improve mucus clearance

INVENTOR(S): King, Malcolm; Speert, David P.

PATENT ASSIGNEE(S): The University of British Columbia, Can.; The

University of Alberta PCT Int. Appl., 32 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

SOURCE:

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KIND DATE
                                             APPLICATION NO. DATE
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     WO 9901141
                             19990114
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             KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
             NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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                                              US 2001-892636
                                                                20010628
                                           CA 1997-2209342 A 19970630
PRIORITY APPLN. INFO.:
                                           CA 1998-2233805 A 19980331
                                                             A1 19980331
                                           US 1998-52614
                                           WO 1998-CA628
                                                             W 19980630
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AB Polysaccharides, e.g. dextran, are used to improve mucus clearance. In the invention, dextran has been shown to reduce viscoelasticity and increase mucus clearability of sputum of cystic fibrosis patients. Dextran also reduces viscoelasticity of healthy dog mucus. The invention therefore may be used to improve mucus clearance in cystic fibrosis patients and treat other conditions assocd. with defect in airway mucus clearance including chronic bronchitis, bronchiectasis, and bronchial asthma.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:539517 HCAPLUS

DOCUMENT NUMBER: 137:103921

TITLE: Use of an LTB4 antagonist for the treatment and/or

prevention of diseases caused by increased expression

of mucin genes

INVENTOR(S): Anderskewitz, Ralf; Meade, Christopher John Montague;

Birke, Franz; Jennewein, Hans Michael; Jung, Birgit

PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma KG, Germany

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2
COCUMENT TYPE: Patent

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

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PATENT NO.
                      KIND DATE
                                             APPLICATION NO. DATE
     _____
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                                             _____
                             20020718 WO 2002-EP200309 20020115
                      A2
     WO 2002055065
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                          GB 2001-1128 A 20010116
US 2001-266833P P 20010206
PRIORITY APPLN. INFO.:
```

AB The invention discloses the use of LTB4 antagonist I or a pharmaceutically acceptable salt thereof for the prepn. of a medicament for the treatment and/or prevention of diseases caused by increased expression of mucin genes and/or hyperplasia of goblet cells induced by toxins of products of pathogenic bacteria in the bronchial or gastrointestinal epithelium.

L77 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2002:332204 HCAPLUS

DOCUMENT NUMBER: 136:345809

TITLE: Mucin-comprising vehicle for the transport of

biologically-active agents

INVENTOR(S): Shukla, Ashok Kumar; Shukla, Mukta M.; Shukla, Amita

M. USA

PATENT. ASSIGNEE(S): US

SOURCE: PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PAT	PATENT NO.			KI	ND	DATE			APPLICATION NO.						DATE			
WO	2002	0347 JP	63	 A:	2	2002	0502		V	10	200)1-U	S501	52	20011026			
			•	•	CY,	DE,	DK,	ES,	FI,	F	R,	GB,	GR,	IE,	IT,	LU,	MC,	NL,
US	6320	,	01,	В	_	2001							9689		2000			
US	2002	0907:	21	A	1	2002	0711		Ţ	JS .	200	1-7	5486	-	2001			
US	2002	0990	05	A	1	2002	0725		Ţ	JS .	200	1-7	6746	2	2001	0123		
PRIORITY	APP:	LN.	INFO	. :				1	US 2	005	0-6	5968	97	Α	2000	1026		
								1	US 2	200	1-7	7548	68	Α	2001	0105		
								1	US 2	009	1-7	7674	62	Α	2001	0123		

AB A vehicle for the transport of biol. active or therapeutic agents into

organisms, such as human beings, comprising mucin is described. The mucin component of the vehicle serves to enhance the transport of biol. active agents, such as therapeutic agents into living organisms; to control and/or improve the delivery of biol. active agents to cells, tissues, organs or organelles; to increase the level of specificity in targeting particular cells or cells types; and/or, to enhance the activity of such therapeutic agents once they enter an organism. The vehicle described in the present invention is used to carry and deliver biol. active agents and can be used for biochem., therapeutic, clin., or other applications in organisms and cells including, but not limited to, delivery of DNA, RNA, PNA, polynucleotides and proteins into cells, tissues or organisms; gene delivery applications; in vivo gene therapy, ex vivo gene therapy or in vitro gene therapy; customized therapeutics; vaccination of organisms; genetic vaccination of organisms; and delivery of pharmaceutical products or biol. active chem., biochem. or biol. agents into cells and organisms.

L77 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2002 ACS 2002:616204 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

TITLE:

137:168277

Detection and treatment of cancer

INVENTOR(S):

Moro, Ricardo J.

PATENT ASSIGNEE(S):

Can.

SOURCE:

U.S. Pat. Appl. Publ., 23 pp., Cont. of U.S. Ser. No.

920,654.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. ______ _____ US 2001-848141 20010503 US 2002110556 A1 20020815 US 1997-920654 A1 19970815 PRIORITY APPLN. INFO.:

A method is described for treating cancer cells in a patient. The method comprises the steps of introducing .alpha.-fetoprotein (AFP) receptor antibodies to cancer cells in the patient. Then there is the step of reacting the AFP receptor antibodies with the AFP receptor of the cancer cells to inhibit growth of the cancer cells or kill the cancer cells.

L77 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:564827 HCAPLUS

DOCUMENT NUMBER:

135:147436

TITLE:

INVENTOR(S):

Mucin synthesis inhibitors and their therapeutic use Zhou, Yuhong; Levitt, Roy C.; Nicolaides, Nicholas C.;

Jones, Steve; McLane, Mike

PATENT ASSIGNEE(S):

Magainin Pharmaceuticals, Inc., USA

SOURCE:

PCT Int. Appl., 59 pp.

DOCUMENT TYPE:

CODEN: PIXXD2

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

APPLICATION NO. DATE KIND DATE PATENT NO. -----_____ ____ WO 2001054685 A1 20010802 WO 2001-US3078 20010131 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,

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TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
              MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                              US 2001-774243
                                                                 20010131
     US 2001041685
                       Α1
                              20011115
                                           US 2000-179127P P 20000131
PRIORITY APPLN. INFO.:
                                           US 2000-193111P P 20000330
                                           US 2000-230783P P 20000907
                                           US 2000-242134P P 20001023
                                           US 2000-252052P P 20001120
                           MARPAT 135:147436
OTHER SOURCE(S):
     Methods are provided for modulating mucin synthesis and the therapeutic
     application of compds. in controlling mucin over-prodn. assocd. with
     diseases such as chronic obstructive pulmonary diseases (COPD), including
     asthma and chronic bronchitis, inflammatory lung diseases, cystic fibrosis
     and acute or chronic respiratory infectious diseases.
                                 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
                           2
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L77 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2002 ACS
                           2001:435244 HCAPLUS
ACCESSION NUMBER:
                           135:42763
DOCUMENT NUMBER:
                           Purification, characterization and therapeutic and
TITLE:
                           diagnostic use of leukolysin
INVENTOR(S):
                           Pei, Duanqing
                           Regents of the University of Minnesota, USA
PATENT ASSIGNEE(S):
                           PCT Int. Appl., 98 pp.
SOURCE:
                           CODEN: PIXXD2
DOCUMENT TYPE:
                           Patent
LANGUAGE:
                           English
FAMILY ACC. NUM. COUNT:
                           1
PATENT INFORMATION:
                                              APPLICATION NO. DATE
     PATENT NO.
                      KIND DATE
                                              ______
                       ____
     _____
     WO 2001042438 A2
                                             WO 2000-US33763 20001213
                              20010614
                       A3
                              20020110
     WO 2001042438
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
              YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                           US 1999-170396P P 19991213
PRIORITY APPLN. INFO.:
     A novel compd., matrix metalloproteinase 25 (MM25, also called MT6-MMP or
     leukolysin), and therapeutic methods for treating conditions assocd. with
     the presence or absence of leukolysin is provided. Leukolysin was
     identified from human peripheral blood leukocytes and found to be
     specifically expressed by resting neutrophils. Leukolysin encodes for 562
     residues with common MMP domains. Amino acid sequence of leukolysin is
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L77 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:258908 HCAPLUS

physiol. sample.

provided. Leukolysin expression at the mRNA level was localized to neutrophils only. Also provided are methods to detect or monitor inflammatory disease by detg. the presence or amt. of leukolysin in a

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DOCUMENT NUMBER:
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CORPORATE SOURCE:

135:221222

TITLE:

Nebulized heparin in Burkholderia cepacia colonized

adult cystic fibrosis patients

AUTHOR(S):

Ledson, M.; Gallagher, M.; Hart, C. A.; Walshaw, M.

The Regional Adult Cystic Fibrosis Unit, The

Cardiothoracic Centre, Liverpool, UK

SOURCE:

European Respiratory Journal (2001), 17(1), 36-38

CODEN: ERJOEI; ISSN: 0903-1936

European Respiratory Society

PUBLISHER: DOCUMENT TYPE:

Journal English LANGUAGE:

Viscous neg. charged cystic fibrosis (CF) sputum allows colonization by AB pathogens, inducing a chronic inflammatory response. Heparin thins sputum by decreasing the mucin mol. amino group neg. charge, altering its intermol. hydrogen bonding, and ionically shielding its polyionic moieties. It also has an anti-inflammatory effect within the lung. may, therefore, be useful in the treatment of CF patients. In order to test this, six fully informed Burkholderia cepacia colonized stable adult CF patients, received 25,000 IU nebulized heparin sulfate daily for 7 days. Subjective sputum parameters, spirometry, platelets, coagulation parameters, and serum and sputum interleukin (IL)-6 and -8 were measured before and after treatment. All patients tolerated the heparin with no evidence of bleeding, thrombocytopenia or change in coagulation parameters. There was no change in spirometry, but a redn. in interleukins (sputum IL-6, p=0.01; sputum IL-8, p=0.002; serum IL-6, p=0.02; serum IL-8, p=0.02). Sputum was easier to expectorate (p<0.04), with a trend towards thinner sputum (p=0.07) but no change in sputum vol. Heparin therapy was well tolerated and had an anti-inflammatory effect, with subjective sputum mucolysis. Further studies are necessary to define the role of heparin in the treatment of cystic fibrosis patients.

REFERENCE COUNT:

THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS 15 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

2000:608596 HCAPLUS

DOCUMENT NUMBER: INVENTOR(S):

133:187988

TITLE:

Methods and compositions for altering mucus secretion

Li, Yuehua; Martin, Linda D.; Adler, Kenneth B.

PATENT ASSIGNEE(S):

North Carolina State University, USA

SOURCE:

PCT Int. Appl., 66 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO. DATE							
									
WO 2000050062	A2 20000831	WO 2000-US5050 20000224							
	A3 20001221								
W: AE, AL,	AM, AT, AU, AZ, B	A, BB, BG, BR, BY, CA, CH, CN, CU, CZ,							
		E, GH, GM, HR, HU, ID, IL, IN, IS, JP,							
KE, KG,	KP, KR, KZ, LC, L	K, LR, LS, LT, LU, LV, MD, MG, MK, MN,							
MW, MX,	NO, NZ, PL, PT, R	O, RU, SD, SE, SG, SI, SK, SL, TJ, TM,							
TR, TT,	UA, UG, US, UZ, V	N, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,							
RU, TJ,	TM								
RW: GH, GM,	KE, LS, MW, SD, S	L, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,							
DK, ES,	FI, FR, GB, GR, I	E, IT, LU, MC, NL, PT, SE, BF, BJ, CF,							
CG, CI,	CM, GA, GN, GW, M	L, MR, NE, SN, TD, TG							
EP 1154786		EP 2000-912034 20000224							
R: AT, BE,	CH, DE, DK, ES, F	R, GB, GR, IT, LI, LU, NL, SE, MC, PT,							

IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

US 1999-256154 A 19990224 WO 2000-US5050 W 20000224

AB Methods and compds. for increasing or decreasing mucus secretion in subjects, and particularly mucus secretion in the airways, are described. The use of compds. that modulate MARCKS protein-related mucus secretion is described. Methods of screening compds. for the ability to increase or decrease mucus secretion are also described.

L77 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:830323 HCAPLUS

DOCUMENT NUMBER: 134:13334

TITLE: Use of glycosaminoglycans-degrading enzymes for

management of airway associated diseases

INVENTOR(S): Yacoby-Zeevi, Oron

PATENT ASSIGNEE(S): Insight Strategy & Marketing Ltd., Israel

SOURCE: U.S., 13 pp., Cont.-in-part of U.S. 5,968,822.

CODEN: USXXAM

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT	NO.				DATE							0.	DATE			
US 6153	187		 А		2000	1128				98-4			1998	0325		
US 5968	822		Α		1999	1019		U.	S 19	97-92	2217	0	1997	0902		
US 2002					2002	0530		U:	S 19	98-1	4088	8	19980	0827		
US 6423			В		2002											
US 2001								U	S 19	99-2	6003	7	19990	0302		
WO 9948			A										19990			
W:	ΑE,														CU,	CZ,
													ID,			
													LV,			
													SI,			
													AZ,			
					00,	05,	04,	V 14,	10,	217,		1111,	114,	D1,	110,	112,
DW.	GH,		TJ,		N/ITA7	e D	CT	C 7	пс	77 TAT	ייי ע	PF	CH	CV	DE	DK
EW.																
			•	•								SE,	BF,	ъυ,	Cr,	CG,
					GW,											
AU 9931																
US 2002	0880	19	A.	1	2002	0704		U	S 20	01-9	7829	7	2001	1017		
PRIORITY APE	LN.	INFO	.:					US 1	997-	9221	70	Α2	1997	0902		
								US 1	998-	4647	5	A1	19980	0325		
								US 1	998-	14088	88	A2	19980	0827		
							•	US 1	999-	2600	37	A2	19990	0302		
							,	WO 1	999-	US618	8 9	W	19990	0322		
													2000			
7D D:1					£									_	ion	o f

AB Disclosed is a method of managing a patient having an accumulation of mucoid, mucopurulent or purulent material contg. glycosaminoglycans, wherein the method comprises the step of administering at least one glycosaminoglycans degrading enzyme to the patient in an amt. therapeutically effective to reduce at least one of the following: the viscoelasticity of the material, pathogens infectivity and inflammation. An article of manuf. comprising an inhaler including, as an active ingredient, at least one glycosaminoglycans degrading enzyme for generating aerosols including the enzyme for management a patient having an accumulation of mucoid, mucopurulent or purulent material contg. glycosaminoglycans is also disclosed. Sputum samples collected from cystic fibrosis patients were incubated with heparinase II and DNase for examine the changes of viscosities of the sputum samples during the

incubation.

AUTHOR(S):

AB

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:528183 HCAPLUS

DOCUMENT NUMBER: 133:359052

TITLE: Effects of dextran sulfate on tracheal

mucociliary velocity in dogs
Sudo, E.; Boyd, W. A.; King, M.

CORPORATE SOURCE: Pulmonary Research Group, University of Alberta,

Edmonton, AB, Can.

SOURCE: Journal of Aerosol Medicine (2000), 13(2), 87-96

CODEN: JAEMEP; ISSN: 0894-2684

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

We have shown that low mol. wt. dextran, as a potential mucolytic agent, reduced the viscoelasticity and spinnability of cystic fibrosis (CF) sputum and improved its ciliary transportability in vitro; it also reduced viscoelasticity of healthy dog mucus in in vitro testing. In anesthetized dogs, dextran administered by aerosol at 65 mg/mL increased tracheal mucus velocity, but this increase was not sustained for higher concns. The purpose of the present study is to evaluate whether low mol. wt. dextran sulfate, a charged oligosaccharide, exhibits similar effects to previously tested neutral dextran when administered by aerosol to anesthetized dogs in terms of mucus rheol. and mucociliary clearance rate. Healthy mongrel dogs were anesthetized with pentobarbital and intubated. Aerosols of Ringer's soln. or dextran sulfate (m.w. 5000) dissolved in Ringer's were generated by Pari LC STAR nebulizer, and delivered during 30-min periods of spontaneous breathing. Tracheal transepithelial p.d. (PD, using agar filled electrodes) and tracheal mucociliary velocity (TMV, by charcoal marker particle transport) were measured under bronchoscopic control, and mucus for viscoelasticity anal. by magnetic rheometry was collected by the endotracheal tube method. We performed expts. in seven dogs, involving 30-min administrations of aerosol, sepd. by 30-min periods of no aerosol. All dogs received inhalations of 6.5 mg/mL, 20 mg/mL, and 65 mg/mL dextran sulfate. Tracheal mucus viscoelasticity (av. log G* over 1-100 rad/s) decreased progressively with increasing dose of dextran sulfate; for the highest concn. (65 mg/mL), log G* decreased by a factor of 2.61 (p = 0.021). A modest increase in the TMV was obsd. for the first dose of dextran sulfate (128% of baseline at 6.5 mg/mL, p = 0.066); thereafter TMV was stable. PD increased significantly at each concn. of dextran sulfate compared with Ringer control; however, there was no addnl. change between the three groups. The solids content of collected airway fluid (%SC) was gradually increased during successive 30-min dextran sulfate aerosols, indicating a significant residence time for the dextran in the mucus, and correlating with the decrease in viscoelasticity. results suggest that dextran sulfate may be potentially of therapeutic value as a mucolytic agent, assisting mucus clearance by cough and physiotherapy, although whether it stimulates mucociliary clearance remains to be proven.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L77 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1999:626027 HCAPLUS

DOCUMENT NUMBER: 131:252572

TITLE: Use of qlycosaminoglycan-degrading enzymes for

management of airway-associated diseases

INVENTOR(S):

Yacoby-Zeevi, Oron

PATENT ASSIGNEE(S):

Insight Strategy & Marketing Ltd., Israel; Friedman,

Mark M.

SOURCE:

PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

15

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA	PATENT NO.					KIND DATE			A.	PPLI	CATI	N NC	0.	DATE			
WO	9948	 478		A	1	1999	0930		W	0 19	99-U	s618	9	1999	0322		
	W:	ΑE,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CU,	CZ,
		DE,	DK,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,
		JP,	ΚĖ,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	MD,	MG,	MK,
		MN,	MW,	MX,	NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,
		TM,	TR,	TT,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,
		MD,	RU,	ТJ,	MT												
	RW:	GH,	GM,	ΚE,	LS,	MW,	SD,	SL,	SZ,	UG,	ZW,	AT,	BE,	CH,	CY,	DE,	DK,
		ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,
		CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG					
US	6153	187		Α		2000	1128		U	S 19	98-4	6475		1998	0325		
AU	9931	077		Α	1	1999	1018		A	U 19	99-3	1077		1999	0322		
PRIORIT	Y APP	LN.	INFO	.:					US 1	998-	4647	5	Α	1998	0325		
								US 1997-922170 A2 19970902									
										WO 1999-US6189 W 19990322							

A method of managing a patient having an accumulation of mucoid, AB mucopurulent, or purulent material contg. glycosaminoglycans comprises administering at least one glycosaminoglycan-degrading enzyme to the patient in an amt. therapeutically effective to reduce at least one of the following: the viscoelasticity of the material, pathogen infectivity, and inflammation. An article of manuf. is provided which comprises an inhaler including, as an active ingredient, at least one glycosaminoglycandegrading enzyme for generating aerosols including the enzyme for management of a patient having an accumulation of mucoid, mucopurulent, or purulent material contg. glycosaminoglycans.

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L77 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                        1998:223988 HCAPLUS
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DOCUMENT NUMBER:

129:555

TITLE:

Heparin accelerates the inhibition of cathepsin G by

mucus proteinase inhibitor: potent effect of

O-butyrylated heparin

AUTHOR(S):

Ermolieff, Jacques; Duranton, Jerome; Petitou,

Maurice; Bieth, Joseph G.

CORPORATE SOURCE:

Laboratoire d'Enzymologie, INSERM Unite 392,

Universite Louis Pasteur de Strasbourg, Illkirch,

F-67400, Fr.

SOURCE:

Biochemical Journal (1998), 330(3), 1369-1374

CODEN: BIJOAK; ISSN: 0264-6021

PUBLISHER:

Portland Press Ltd.

DOCUMENT TYPE:

Journal

LANGUAGE: English

AB Heparin tightly binds cathepsin G and so protects the enzyme from inhibition by .alpha.1-antichymotrypsin, .alpha.1-proteinase inhibitor and eglin c, three proteins which do not bind heparin [Ermolieff J., Boudier C., Laine A., Meyer B. and Bieth J. G. (1994) J. Biol. Chem. 269,

29502-29508]. Here we show that heparin no longer protects cathepsin G from inhibition when the enzyme is reacted with mucus proteinase inhibitor (MPI), a heparin-binding protein. Heparin fragments of Mr = 4500 and 8100 and O-butyrylated heparin of Mr = 8000 form tight complexes with cathepsin G (Kd = 0.5-2.2 nM) and MPI (Kd = 0.4-0.8 .mu.M) and accelerate the MPI-promoted inhibition of cathepsin G by a factor of 17-26. They also accelerate the inhibition of neutrophil elastase and pancreatic chymotrypsin. The rate acceleration is due to the binding of heparin to MPI. Butyrylation of heparin slightly decreases its affinity for cathepsin G and MPI but sharply decreases the ionic interactions between the pos. charged proteins and the neg. charged polyanion. The butyrylated heparin deriv. is the best rate accelerator: it increases the rate const. for the MPI-induced inhibition of cathepsin G and elastase by factors of 26 and 23, resp. This, together with the fact that it has a good bioavailability and a very low anticoagulant activity, suggests that it might be an adjuvant of MPI-based therapy of cystic fibrosis.

L77 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2002 ACS

1997:107949 HCAPLUS ACCESSION NUMBER:

126:210579 DOCUMENT NUMBER:

Transcriptional activation of mucin by Pseudomonas TITLE:

aeruginosa lipopolysaccharide in the pathogenesis of

cystic fibrosis lung disease

Li, Jian-Dong; Dohrman, Austin F.; Gallup, Marianne; AUTHOR(S):

Miyata, Susumu; Gum, James R.; Kim, Young S.; nadel,

Jay A.; Prince, Alice; Basbaum, Carol B.

Department Anatomy, University California, San CORPORATE SOURCE:

Francisco, CA, 94143, USA

Proceedings of the National Academy of Sciences of the SOURCE:

United States of America (1997), 94(3), 967-972

CODEN: PNASA6; ISSN: 0027-8424

National Academy of Sciences PUBLISHER:

DOCUMENT TYPE: Journal English LANGUAGE:

An unresolved question in cystic fibrosis (CF) research is how mutations of the CF transmembrane conductance regulator, a Cl ion channel, cause airway mucus obstruction leading to fatal lung disease. Recent evidence has linked the CF transmembrane conductance regulator mutation to the onset and persistence of Pseudomonas aeruginosa infection in the airways, and here the authors provide evidence directly linking P. aeruginosa infection to mucus overprodn. The authors show that P. aeruginosa lipopolysaccharide profoundly upregulates transcription of the mucin gene MUC 2 in epithelial cells via inducible enhancer elements and that this effect is blocked by the tyrosine kinase inhibitors genistein and tyrphostin AG 126. These findings improve the authors' understanding of CF pathogenesis and suggest that the attenuation of mucin prodn. by lipopolysaccharide antagonists and tyrosine kinase inhibitors could reduce morbidity and mortality in this disease.

L77 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1993:462774 HCAPLUS

119:62774 DOCUMENT NUMBER:

یا رسم بند دید به است. داند استون بدادندی بسی کند، چه دادی Medicinal use of polysaccharide-of-exocarpium citri TITLE:

Zhou, Bowen; Hu, Wenya; Wu, Junjing AUTHOR(S):

1st Affil. Hosp., Zhongshan Med. Univ., Guangzhou, CORPORATE SOURCE:

510080, Peop. Rep. China

Zhongguo Yaoxue Zazhi (Beijing, China) (1993), 28(3), SOURCE:

135-6

CODEN: ZYZAEU; ISSN: 1001-2494

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Pharmacol. studies indicated that polysaccharides of Citrus grandis have antitussive and expectorant actions in mice and have therapeutic effects against chronic bronchitis and pulmonary obstructive emphysema in humans.

L77 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 1992:604956 HCAPLUS

DOCUMENT NUMBER: 117:204956

TITLE: Effects of ambroxol hydrochloride on the guinea pig

tracheal mucous secretion and the rat pulmonary

surfactant secretion

AUTHOR(S): Uchida, Masayuki; Noguchi, Yuji; Arakawa, Reijiroh;

Hashimoto, Yoshiko; Ikarashi, Yasuko; Honda, Hideo

CORPORATE SOURCE: Pharmacol. Res. Lab., Grelan Pharm. Co., Ltd., Tokyo,

154, Japan

SOURCE: Nippon Yakurigaku Zasshi (1992), 100(4), 293-300

CODEN: NYKZAU; ISSN: 0015-5691

DOCUMENT TYPE: Journal LANGUAGE: Japanese

AB Oral administration of ambroxol (10, 30, and 100 mg/kg) significantly increased the no. of active goblet cells in guinea pig tracheal epithelium and total mucopolysaccharide level. Ambroxol also significantly increased the neutral mucopolysaccharide level and PAS-pos. substance in the guinea pig tracheal submucosal glands. Ambroxol did not show a significant effect on the content of the total phosphatidylcholine in rat lung lavage fluid, while ambroxol significantly increased the ratio of disatd. phosphatidylcholine to total phosphatidylcholine. These results suggest that ambroxol increases both the tracheal mucous secretion, esp. the neutral mucopolysaccharide, and pulmonary surfactant secretion and these effects reflect part of the expectorant mechanism of the drug.

L77 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:441697 HCAPLUS

DOCUMENT NUMBER: 115:41697

TITLE: Evaluation of bronchospasmolytic, antiallergic,

anti-inflammatory, mucolytic and antitussive activities of decasilate in experimental models Ucelay, M.; Labeaga, L.; Orjales, A.; Zubiaur, L.;

Quintana, A.

CORPORATE SOURCE: Res. Dep., FAES S. A., Bilbao, E-48080, Spain

SOURCE: Arzneim.-Forsch. (1991), 41(5), 528-32

CODEN: ARZNAD; ISSN: 0004-4172

DOCUMENT TYPE: Journal LANGUAGE: English

AUTHOR(S):

The bronchospasmolytic, antiallergic, anti-inflammatory, mucolytic and antitussive activities of decasilate (I) have been evaluated using different exptl. models. Decasilate showed a remarkable spasmolytic activity against histamine-induced contractions in the isolated guinea-pig tracheal prepn. with an IC50 of 2.7 .times. 10-6 mol/L. In addn., the oral administration of decasilate (5-30 mg.kg-1) significantly reduced the histamine aerosol-induced bronchospasm in guinea-pigs. Decasilate had a preventive effect against antigen-induced contractions of ileum segments from sensitized guinea-pigs (EC50 8.0 .times. 10-6 mol/L) and relaxed then when added after the antigen challenge (IC50 9.5 .times. 10-7 mol/L). Both carrageenin- and dextran-induced rat hind paw edemas were significantly reduced by the oral administration of decasilate with ED50 values of 169.5 and 34.5 mg.kg-1, resp. However, it was ineffective against the cotton pellet-induced granuloma in the rat. Furthermore, decasilate had a significant mucolytic activity in rabbits and reduced the no. of tussive seizures induced by an aerosol of citric acid in quinea-pigs. The pharmacol. profile of decasilate suggests that it might

Khare 09/892,636

Page 18

be useful in the management of chronic bronchitis.

L77 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1991:129110 HCAPLUS

DOCUMENT NUMBER:

114:129110

TITLE:

Dual-action pharmaceutical tablet

INVENTOR(S):

Dansereau, Richard John; Kane, Michael John

PATENT ASSIGNEE(S):

Norwich Eaton Pharmaceuticals, Inc., USA

SOURCE:

Eur. Pat. Appl., 9 pp.

DOCUMENT TYPE:

CODEN: EPXXDW

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

	PAT	ENT N	Ю.		KIN	ID	DATE			P	APP	LICA)ITA	N NC	Ο.	DATE	
		38451			A2		1990			E	P.	1990) - 2(0031	3	1990	0212
	EΡ	38451	. 4		A3	3	1991										
	EΡ	38451	. 4		В1	-	1993	1124									
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	G	R, I	ľΤ,	LI,	LU,	NL	
	US	50324	06		Α		1991	0716		Ü	IS	1989	9-31	1467	2	1989	0221
	ΑT	97571			E		1993	1215		P	T	1990)-20	0031	3	1990	0212
	ES	20609	23		ТЗ	3	1994	1201		E	S	1990	0-20	0031	3	1990	0212
	CA	20100	37		AP	1	1990	0821		C	A	1990	0-20	100	37	1990	0214
	CA	20100	37		С		1995	1031									
	ΑU	90499	70		A1		1990	0830		Z.	U	1990)-49	970		1990	0220
	AU.	63279	13		В2		1993	0114									
	ZA	90012	61		Α		1990	1128		Z	Ά	1990)-12	261		1990	0220
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	JΡ	28951	46		В2		1999	0524									
RIOF	RITY	APPL	N. 3	INFO.	:				Ţ	JS 1	98	9-33	1467	72		1989	0221
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The title tablet comprises (1) an outer tablet of a 1st dose of active AR ingredient dispersed in a pH-independent hydrophilic polymer matrix, and (2) an inner tablet of a 2nd dose of active ingredient in a rapidly disintegrating excipient base. The dual-action tablet is esp. efficacious for those active ingredients of half-lives <2 h and which experience decreased absorption efficiency in the lower gastrointestinal tract. On administration, the outer tablet provides a controlled-release of active ingredient while the inner tablet gives a 2nd dose of active ingredient after the outer tablet has partially dissolved. An expectorant compn. contains (1) an inner tablet of guaifenesin 175.0, microcryst. cellulose 35.1, crosspovidone 35.0, polyvinylpyrrolidone 7.3, talc 2.3, and Zn stearate 2.3 mg; and (2) an outer tablet of guaifenesin 425.0, hydroxypropylmethyl cellulose K4M 139.9, stearic acid 30.0, and Zn stearate 5.4 mg. Dual action tablets for administration of procainamide-HCl and of KCl (for K supplementation) are also described.

L77 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1990:16254 HCAPLUS

DOCUMENT NUMBER:

112:16254

TITLE:

P

Targeted delivery of drugs and diagnostic agents using carriers which promote endothelial and epithelial

uptake and lesional localization

INVENTOR(S):

Ranney, David F.

PATENT ASSIGNEE(S):

USA

SOURCE:

PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1 PATENT INFORMATION:

	PA'	rent 1	NO.		KI	ND	DATE			Į	APPLI	CATI	ON NO	Э.	DATE			
		8807 8807					1988 1988			V	vo 19	88-U	S109	6	1988	0330		
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		RW:		-	•		CG,	CH,	CM,	DE,	FR,	GA,	GB,	IT,	LU,	ML,	MK,	NL,
	FIC	4925	•	SN,	•		1 9 9 0	N515		г	IS 10	87-3	3432		1987	0401		
		8816									-				1988			
		6074					1991	-		•	10 13	00 1	0270		1300	0000		
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Targeted delivery systems comprise drugs or diagnostic agents and carriers AΒ which recognize determinants present on normal or diseased endothelium. This induces the following effects in vivo: (1) rapid endothelial envelopment of the carrier; (2) sequestration of the carrier and protection of the entrapped agent from early blood clearance; (3) acceleration of the carrier's transport across the vascular endothelium into the interstitium; and (4) improvement of drug delivery across the endothelium, so that a lower total drug dose is required. Aq. cisplatin (I) was mixed with heparin at a 1:1.1 wt. ratio and ultrasonicated to form a heparin-coated I microemulsion with particle sizes of 0.2-1.5 .mu.m, which was stable for >1 h at 22.degree.. Mice receiving this emulsion i.v. showed moderate to intense concn. of I in the lung interstitia, alveolar pneumocytes, respiratory epithelia, and lymph nodes, but low I concns. in the liver, whereas mice receiving std. aq. I showed intense I concn. in the liver and almost no I in the lungs. Thus high concns. of I (which are usually toxic to endothelium) can be successfully reformulated as a heparin microemulsion, and the heparin component can induce endothelial binding and transcellular uptake of the complexes in a fashion that protects the endothelium from the toxic effects of the drug.

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L77 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2002 ACS
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ACCESSION NUMBER: 1988:62482 HCAPLUS

DOCUMENT NUMBER: 108:62482

TITLE: Pharmaceutical compositions for inhalation containing

an excipient from microgranules of a conglomerate of solid water-soluble diluents and a lubricant for

bronchopulmonary disorders

INVENTOR(S): Chiesi, Paolo; Pavesi, Luciana PATENT ASSIGNEE(S): Chiesi Farmaceutici S.p.A., Italy

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PAT	TENT	NO.		KI	ID	DATE									DATE	3		
			5213 AU,	BB,	BG,	BR,				W	0 1		EP11	L8					RO,
	AU	8773	1645	SU,	A]		19870	0928		А	U 1	987-	7164	15		1987	0227		
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	EΡ	2397	798		A		1987	1007		Ε	P 1	987-1	1028	316		1987	0227		
			798																
		R:	ES,	GR															
	ΕP	2583	356		A.		19880	0309		E	P 1	987-9	9014	168		1987	0227		
			356														•		
		R:	AT,	BE,	CH,	DE,	FR,	GB,	IT,	LI,	LU	, NL	, SE	E					
	JP	6350	02895		T2	2	19883	1027		J	P 1	987-	5019	911		1987	0227		
	HU	4653	33		A2	2	19883	1128		Н	U 1	987-3	1760)		1987	0227		
	HU	202	33 748 1839		В		1991	0429											
	ES	2033	1839		Т3	3	19930	0101		Ε	S 1	987-3	1028	316		1987	0227		
	AT	9475	55		E		1993.	1015		Α	T 1:	987-9	9014	168		198/	0227		
	zA	8703	1523		· A		1987	1028		Z	A 1	987-1	1523	3		1987	0303		
	CA	129	7012		A.		19920	0310		С	A 1	987-5	5310)54		1987	0303		
	FI	8704	4710 15 15		A		1987	1026		F	I 1	987-4	4710)		1987	1026		
	FI	900	15		В		19930	0915											
	FI	900	15		С		1993	1227											
	NO	8704	4590		Ζ\		1987	1230		N	0 1	987-	159r)		1987	71103		
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									E	3P 1	987	-901	468			198/	0221		
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AΒ Powders for inhalation are provided with microgranules of a conglomerate of .gtoreq.1 solid H2O-sol. diluents and a lubricant. Beclomethasone dipropionate with lactose conglomerated with Mg stearate or with com. available microcryst. lactose was tested in 2 groups of inhaler devices. In the case of the conglomerate, the residual quantity of powder required to enable a wt. distribution within acceptable limit was lower (300 mg) than that required with the simple microcryst. excipient (500 mg).

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L77 ANSWER 22 OF 32 WPIDS (C) 2002 THOMSON DERWENT
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ACCESSION NUMBER: 2002-303912 [34]

DOC. NO. CPI:

C2002-088337

TITLE:

Treatment of allergies, autoimmunity, adhesion

cascade, metastatic or coronary cascade diseases e.g. arthritis comprises administration of at least one

complex carbohydrate e.g. chondroitin sulfate.

DERWENT CLASS:

A96 B04 D21 BROWN, H G; BROWN, K K; COOPER, C A INVENTOR(S):

(DERM-N) DERMAL RES LAB INC PATENT ASSIGNEE(S):

96 COUNTRY COUNT:

PATENT INFORMATION:

PATENT	NO	KIND	DATE	WEEK	LA	PG

WO 2002009728 A1 20020207 (200234)* EN 61

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU

SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001081368 A 20020213 (200238)

APPLICATION DETAILS:

ITII BUIL ING I	KIND		PLICATION	DATE
WO 2002009728 AU 2001081368	3 A1	WO	2001-US41473 2001-81368	20010731

FILING DETAILS:

PATENT NO PATENT NO KIND _____ WO 200209728 AU 2001081368 A Based on

PRIORITY APPLN. INFO: US 2000-222046P 20000731 WO 200209728 A UPAB: 20020528

> NOVELTY - Treatment/prevention of diseases and conditions associated with allergies, autoimmunity, adhesion, metastatic or coronary cascades involves administration of at least one complex carbohydrate or a composition comprising at least one low purity or cosmetic grade complex carbohydrate and at least one transdermal or transmucosal carrier to deliver the complex carbohydrate into the blood stream.

DETAILED DESCRIPTION - Treatment or prevention of diseases associated with allergies, autoimmunity, adhesion cascade, metastatic cascade or coronary cascade involves: administration of at least one complex carbohydrate as sole active ingredient or a composition comprising at least one low purity or cosmetic grade complex carbohydrate as an active ingredient and at least one transdermal or transmucosal carrier to deliver the complex carbohydrate into the blood stream. The complex carbohydrate is oligosaccharide, sialylated oligosaccharide, polysaccharide or glycosaminoglycan.

INDEPENDENT CLAIMS are also included for the following:

- (1) interrupting the adhesion cascade by blocking the ability of leukocyte to bind to blood vessel walls, involving contacting the complex carbohydrate with receptor sites on leukocytes to inhibit the ability of the leukocyte to bind to the blood vessel walls to inhibit the motility to the site of trauma and thus reducing pain and swelling;
- (2) a bandage comprising either at least one complex carbohydrate and the carrier resulting in topical or mucosal delivery of the molecules, through the skin or mucous membranes of mammals and into the bloodstream or comprising only the complex carbohydrate added to it or imbedded in it. The bandage is applied onto an area requiring treatment;
- (3) blocking the ability of tumor cells to tether to blood vessel walls by contacting the complex carbohydrates with receptor sites on tumor cells to inhibit the ability of the tumor cells to bind to the blood vessel walls and inhibit the tumor motility which, in turn, inhibits the potential for metastasis.

ACTIVITY - Immunosuppressive; Antiarthritic; Antirheumatic; Antiinflammatory; Antiulcer; Virucide; Antiallergic; Nootropic; Dermatological; Vasotropic; Vulnerary; Analgesic; Gynecological; Antiasthmatic; Antipruritic; Thrombolytic; Anticonvulsant; Tranquilizer; Neuroleptic; Neuroprotective; Antiparkinsonian; Cerebroprotective; Hypotensive; Cardiant; Anticoagulant; Anti-HIV; Antibacterial; Virucide; Antiseborrheic; Cytostatic; Antidiabetic; Antidepressant; Osteopathic.

MECHANISM OF ACTION - Macrophage inhibitor; T-cell inhibitor; Metastasis inhibitor; Tumor cell blocker; Amyloid plaque inhibitor; Leukocyte (CD44 and CD31) and RHAMM agonist; Leukocyte inhibitor.

USE - In the treatment of diseases associated with allergies, autoimmunity, adhesion cascade, metastatic cascade or coronary cascade e.g. arthritis, gastritis, colitis, stomach or intestinal ulcer, esophagitis, bronchitis, common cold, rhinitis, sore throat, tonsillitis, tendonitis, fibromyalgia, chronic fatigue syndrome,

interstitial cystitis, polymyositis, autism, Lupus Erythematosis, headache, pancreatitis, anaphylaxis, vaginitis, hemorrhoids, sunburn, heat burn, temporomandibular joint (TMJ) condition, gingivitis, dental caries, dental pain, post surgical pain, menstrual pain, extremity cramp, pre and post partum pain, itching associated with allergies and hypersensitivity, asthma, emphysema, thrombosis, Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder (ADHD), Turret's Syndrome, multiple sclerosis, Amyotrophic Lateral Sclerosis (ALS) or Lou Gehrig's Disease, Parkinson's Disease, Bell's Palsy, cerebral palsy, peripheral neuropathy, high blood pressure, heart disease, heart attack, vasculitis, stroke, increased degradation of spinal nerves post spinal cord injury, head and brain trauma post injury, encephalitis, epilepsy, Guillain-Barre syndrome, Human Immunodeficiency Virus infection, yeast infections, bacterial infections, viral infections, meningitis, peripheral neuropathy, Creuztfeldt-Jacob Disease, acne, cognitive disorder, adhesion formation post surgery or chemotherapy, scar formation post surgery, non-healing wounds, decubutis ulcers, irritation of nerve ganglion formation, Alzheimer's disease, human immunodeficiency disease, ovarian cancer, lick granulomas, hot spots, eczema, wrinkling of skin, diabetes, scleroderma, skin problems, osteoarthritis, rashes, dementia, pain associated with cervical disc degeneration and hair loss; for inhibiting macrophages; for reducing scar tissue; as bandage (all claimed). Also in the treatment of rheumatoid arthritis, irritated or inflamed muscles, cramped muscles, inflamed tendons, inflamed nerves or nerve bundles (e.g. inflamed ganglion, trigger points), swollen and painful joints, inflamed bladder, bruised tissue, tired feet, open wounds, decubitis ulcers, inflamed stomach or intestinal lining, inflamed bronchi or esophagial lining, adhesions formed after surgery, trauma or chemotherapy, pain post surgery, dental work or injury, plaques formed on veins or arteries leading to heart disease and stroke, inflammation associated with Alzheimer's Disease, head or brain trauma, degration of the spinal cord post spinal cord injury, pain associated with insect bites or stings, tumor formation and tumor metastasis. The composition stimulates the healing of open wounds, increases cognitive function, thickens hair and fingernails, increases suppleness of skin.

ADVANTAGE - The method does not require pharmaceutical grade complex carbohydrates for the administration. As the composition is applied topically, orally, mucosally or parenterally the contaminants do not produce any adverse reactions.

Dwg.0/2

L77 ANSWER 23 OF 32 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-164495 [21] WPIDS

DOC. NO. CPI: C2002-050810

TITLE: Pharmaceutical composition useful for treating a

respiratory disorder e.g. cystic fibrosis, asthma comprises dextrin.

DERWENT CLASS: B04

INVENTOR(S): ALTON, E; STERN, M

PATENT ASSIGNEE(S): (INNO-N) INNOVATA BIOMED LTD

COUNTRY COUNT: 96

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002002126 A1 20020110 (200221)* EN 22

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU

SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AU 2001069263 A 20020114 (200237)

APPLICATION DETAILS:

PATENT NO K	IND	AP	PLICATION	DATE
WO 2002002126	7.1		2001-GB2887	20010702
AU 2001069263			2001-69263	20010702

FILING DETAILS:

AB

PATENT NO	KIND			PAT	ENT	NO	
AU 200106926	53 A	Based	on	WO	2002	20212	26

PRIORITY APPLN. INFO: GB 2001-1414 20010119; GB 2000-16133

20000701 WO 200202126 A UPAB: 20020403

presence of saline.

NOVELTY - A pharmaceutical composition (A) comprises dextrin. ACTIVITY - Cytostatic; Antiinflammatory; Antiasthmatic; Antibacterial.

The growth of the clinical strains of mucoid and non-mucoid Pseudomonas aeruginosa were treated with solutions of icodextrin (test) and mannitol (comparative) in phosphate buffer solution (PBS). The results for the bacterial cell growth inhibition expressed as % change for 5, 50 and 250 mg/ml of icodextrin/mannitol, when compared to control samples in which the bacteria were incubated with PBS alone were as follows: For non-mucoid Pseudomonas aeruginosa = 26/93, 4/85, -11/92; for mucoid Pseudomonas aeruginosa =11/104, 8/91, -34/76. Thus it was observed that icodextrin had an inhibitory effect while bacteria proliferated in the

MECHANISM OF ACTION - Airway surface liquid water absorption promoter.

USE - In the treatment of respiratory disorders e.g. cystic fibrosis (claimed), chronic bronchitis, asthma and bronchiectasis.

ADVANTAGE - The composition enhances water absorption in airway surface liquid and promotes the mucus clearance. Thus avoids the bacterial incubation in the mucus and subsequent infections responsible for the respiratory disorders. The composition is also effective against the non-mucoid organisms. Dwg.0/0

L77 ANSWER 24 OF 32 WPIDS (C) 2002 THOMSON DERWENT

2001-582010 [65] WPIDS ACCESSION NUMBER:

C2001-172535 DOC. NO. CPI:

Adjuvant composition for modulating effect of medicinal TITLE:

> substances administered onto mucosal surfaces for treating allergy, comprises polysaccharide with glucose monomers linked by beta-1,3 and

beta-1,6 linkages.

B01 B04 D16 DERWENT CLASS:

BAKKE, H; BERSTAD, A K H; HANEBERG, B; HAUGEN, I L; INVENTOR(S):

HOLST, J; JANAKOVA, L; KORSVOLD, G E; OFTUNG, F; RAA, J (BIOT-N) BIOTEC ASA; (BAKK-I) BAKKE H; (BERS-I) BERSTAD A

PATENT ASSIGNEE(S): K H; (HANE-I) HANEBERG B; (HAUG-I) HAUGEN I L; (HOLS-I)

HOLST J; (JANA-I) JANAKOVA L; (KORS-I) KORSVOLD G E;

(OFTU-I) OFTUNG F; (RAAJ-I) RAA J

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2001062283 A2 20010830 (200165) * EN 19

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001040943 A 20010903 (200202) US 2002009463 A1 20020124 (200210)

APPLICATION DETAILS:

PAT	ENT NO K	IND	API	PLICATION	DATE
	2001062283			2001-IB144	20010202
	2001040943 2002009463			2001-40943 2000-511582	20010202 20000223

FILING DETAILS:

PAT	CENT	ИО	KIND			PA'	ENT	NO	
									-
ΑU	2001	104094	3 A	Based	on	WO	2001	162283	

PRIORITY APPLN. INFO: US 2000-511582 20000223

WO 200162283 A UPAB: 20011108

NOVELTY - An adjuvant composition (I), comprising a polysaccharide consisting of glucose monomers linked together in branched chains by beta -1,3 linkages and beta -1,6 linkages which modulate the effect of medicinal substances (II) administered onto mucosal surfaces, is new.

ACTIVITY - Antiallergic; antiarthritic.

MECHANISM OF ACTION - Modulator of (II); vaccine (claimed); modulator of immune reactions to antigens which are in contact with mucosal surfaces in animals and humans.

To investigate the adjuvant effect of the beta -1,3, beta -1,6-glucan preparations, experimental influenza vaccine formulations were compared with regard to their ability to induce specific antibody response and to prime T-cells to proliferate when they were later exposed to vaccine antigens in vitro. The control vaccines contained either heat inactivated whole influenza virus without any adjuvant added or purified antigens of the same virus without adjuvant. The experimental vaccines were made from the same influenza virus vaccine preparations, but admixed with the novel adjuvants. Female BALB/c mice were immunized intranasally with one of the vaccine formulations four times at weekly intervals. The vaccines were administered as drops, with 30 micro 1 dose volumes in the nasal cavity of anesthetized mice. Non-immunized mice served as controls. One week after the last vaccine dose, samples of saliva, serum and spleen cells were collected for analysis of specific antibody responses and antigen specific T-cell proliferation. The results showed that the beta -1,3, beta -1,6-glucan products induced enhanced ability to produce specific antibodies against vaccine antigens which were co-administered onto mucosal surfaces, and furthermore, the beta -1,3, beta -1,6-glucan products primed T-cells in the spleen to respond more actively to later exposure of the same vaccine antigens.

USE - (I) is useful for modulating the effect of medicinal substances administered onto mucosal surfaces. (II) is useful for treating allergy or arthritis. (All claimed). (I) is useful as an adjuvant with vaccines. Dwg.0/0

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L77 ANSWER 25 OF 32 WPIDS (C) 2002 THOMSON DERWENT

2000-514769 [46] ACCESSION NUMBER: WPIDS

C2000-153570 DOC. NO. CPI:

Compositions comprising complex carbohydrates and TITLE: optionally essential oils, useful for preventing or

treating diseases associated with adhesion,

metastatic and coronary cascades.

DERWENT CLASS: B04 D21 D22

BROWN, H G; BROWN, K K; COOPER, C A; HENNESSY, K J INVENTOR(S):

(DERM-N) DERMAL RES LAB INC PATENT ASSIGNEE(S):

COUNTRY COUNT: 91

PATENT INFORMATION:

WEEK PATENT NO KIND DATE T.A PG _____

WO 2000044367 A2 20000803 (200046) * EN 81

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL

OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS

LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL

TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000027457 A 20000818 (200057)

EP 1165097 A2 20020102 (200209) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO K	IND	AP:	PLICATION	DATE
WO 2000044367 AU 2000027457 EP 1165097	• • •	AU EP	2000-US2328 2000-27457 2000-905836 2000-US2328	20000201 20000201 20000201 20000201

FILING DETAILS:

PAT	TENT NO	KIND			PAT	CENT NO
						
ΑU	200002745	7 A	Based	on	WO	200044367
EΡ	1165097	A2	Based	on	WO	200044367

PRIORITY APPLN. INFO: US 1999-166326P 19991119; US 1999-117988P

19990201; US 1999-127749P 19990405; US

19990602; US 1999-142306P 19990703 1999-137098P

AΒ WO 200044367 A UPAB: 20000921

NOVELTY - New composition comprises:

(a) at least one low purity complex carbohydrate selected from oligosaccharides, sialylated oligosaccharides, polysaccharides and glycosaminoglycans as an active ingredient; and

(b) optionally at least one essential oil to allow penetration of the dermis or mucous membranes of mammals by the complex carbohydrate.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) a method of inhibiting the adhesion cascade by administering at least one low purity complex carbohydrate, which blocks the binding of leukocytes to the epithelium during tethering, inhibits migration and extravasation of leukocytes to a site of trauma; and

Page 26

(b) a method of inhibiting tumor formation and tumor metastasis by administering at least one low purity complex carbohydrate, which blocks the metastatic cascade to inhibit binding of tumor cells to the epithelium of blood vessel walls.

ACTIVITY - Antiallergic; dermatological; antiinflammatory; analgesic; antiarthritic; vulnerary; tranquilizer; antiasthmatic; antidiabetic; antiarteriosclerotic; nootropic; neuroprotective; cytostatic; virucide

MECHANISM OF ACTION - Inhibitor of cells binding to epithelium. USE - For treating inflammation, pain or itching, resulting from e.g. arthritis, bursitis, athletic injuries, tendonitis, trauma, gastritis, colitis, esophagitis, bronchitis, sore throat, tonsilitis, tendonitis, fibromyalgia, temporomandibular joint condition, dental pain, bruising, poor circulation, muscle cramps, tired feet, allergies, poison ivy, insect bites/stings, asthma, anaphylaxis, surgery, childbirth, sunburn, burns, edema related to diabetes, debicutus ulcer, superficial cuts, open wounds, dry skin, psoriasis, Attention Deficit Hyperactivity Disorder, plaque formation associated with heart disease and stroke, increased degradation of spinal nerves post spinal cord injury, adhesion formation post surgery, scar formation post surgery, wound healing, ganglion formation, Alzheimer's disease, HIV, cancer, wrinkles, and hair loss. Also for treating or preventing tumors. (All claimed). Dwg.0/0

L77 ANSWER 26 OF 32 WPIDS (C) 2002 THOMSON DERWENT

A96 B04

ACCESSION NUMBER:

TITLE:

1982-10331E--[06] --- WPIDS-Carbohydrate derivs - useful as topical

mucolytic agents non-absorbable by tissues and

free from side effects.

DERWENT CLASS:

INVENTOR(S):

MALTZ, J E

PATENT ASSIGNEE(S):

(TEXC-N) ETAB TEXCONTOR

COUNTRY COUNT:

PATENT INFORMATION:

PAT	TENT NO	KINE	DATE	WEEK	LA	PG
EP	45285	A	∫19820203	(198206)*	EN	27
	R: AT BE	CH	DE GB LI	LU NL SE		
FR	2485925	Α	19820108	(198207)		
JΡ	58013522	Α	19830126	(198310)		
US	4409138	Α	19831011	(198343)		
EΡ	45285	В	19840425	(198418)	EN	
	R: AT BE	CH	DE FR GB	LU NL SE		
DE	3163287	G	19840530	(198423)		
CA	1168169	Α	19840529	(198426)		
US	4559322	Α	19851217	(198602)		
ΙT	1209419	В	19890716	(199136)		

APPLICATION DETAILS:

171111111	KIND	APPLICATION	DATE
EP 45285	Α	EP 1981-830099	19810619
US 4409138	A	US 1983-512679	19830711

PRIORITY APPLN. INFO: IT 1980-23161 19800701 45285 A UPAB: 19930915 AB

Carbohydrate derivs. of formula (I) and of mol. wt. 10000-300000 are new. In (I) A-B is a carbohydrate residue in which A and B are the same or different; Y is a radical to bond the SH to the carbohydrate residue; E is an enzyme radical; R3 is the residue of a functional gp. able to bond the enzyme residue; R2 is a functional gp. to regulate the solubility of the prod., n is 1-2000; m is 0-1000; w is 1-100; and z is 0-10. Each carbohydrate unit is able to carry at least one enzyme residue and at least one SH qp.

Derivs. (I) have topical mucolytic activity esp. on secretions of the respiratory passages; they are not absorbed by the tissues that they contact, but can reach the gastrointestinal tract unaltered. In this tract they are metabolised to non-toxic materials and these can be completely eliminated. They do not have proteolytic effects or allergic side effects and they are compatible with antibiotics. Derivs (I) are useful for topical treatment of bronchial and related afflictions and torpid ulcers, for bladder washing in chronic infections, for treating acne by cleaning cell debris and for eliminating protein and mucopolysaccharide residues in contact lenses.

L77 ANSWER 27 OF 32 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V. DUPLICATE 3

ACCESSION NUMBER: 1999153292 EMBASE

Effects of dextran on tracheal mucociliary velocity in dogs TITLE:

in vivo.

AUTHOR: Feng W.; Nakamura S.; Sudo E.; Lee M.M.; Shao A.; King M.

M. King, Pulmonary Research Group, 173 Heritage Medical CORPORATE SOURCE:

Research Center, University of Alberta, Edmonton, Alta. T6G

2S2, Canada. malcolm.king@ualberta.ca

Pulmonary Pharmacology and Therapeutics, (1999) 12/1 SOURCE:

(35-41).

Refs: 29

ISSN: 1094-5539 CODEN: PPTHFJ

COUNTRY:

United Kingdom Journal; Article

DOCUMENT TYPE:

Chest Diseases, Thoracic Surgery and Tuberculosis FILE SEGMENT: 015

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English English SUMMARY LANGUAGE:

We have previously shown that dextran (molecular weight 4 kDa) is a potential mucolytic agent, reducing the viscoelasticity and spinnability of cystic fibrosis (CF) sputum and improving its mucociliary clearability during in vitro testing. We wished to see whether low molecular weight (LMW) dextran had similar effects on mucus rheology when administered by aerosol to living dogs, and whether the administration of dextran increased the rate of mucociliary clearance. Healthy mongrel dogs mere anesthetized with pentobarbital and intubated. After a 30-min Ringer aerosol delivery during spontaneous breathing, tracheal mucociliary velocity (TMV by charcoal marker particle transport) was measured under bronchoscopic control, and mucus for viscoelasticity analysis (magnetic rheometer) was collected by the endotracheal tube method. Then LMW dextran in Ringer vehicle was delivered by aerosol via the endotracheal tube, followed by the same procedures. We performed eight experiments in eight dogs, involving 30 min administrations of dextran aerosol; all dogs received inhalations of 20 mg/ml, 65 mg/ml, and 200 mg/ml dextran. Compared with Ringer control, TMV increased to 145% of control (P = 0.0417) at 65 mg/ml dextran. Mucus viscoelasticity (G*) significantly decreased to 19% of control (P = 0.0426) at 65 mg/ml. This in vivo study supports our previous in vitro testing that LMW dextran decreases the mucus viscoelasticity and increases the rate of mucociliary clearance. We estimate the dosage received by aerosol at 65 mg/ml to be within the effective concentration range studied in vitro, i.e. 10-15 mg/ml final concentration. The results are consistent with the proposed mechanism that the saccharide moieties in LMW dextran compete for hydrogen bonding sites with other mucous glycoproteins. These new hydrogen bonds are structurally

and theologically ineffective, thus reducing the overall cross-link density, and making the mucus more easily cleared by ciliary and cough mechanisms.

L77 ANSWER 28 OF 32 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001129154 EMBASE

TITLE: Effect of phospholipid mixtures and surfactant formulations

on rheology of polymeric gels, simulating mucus, at shear

rates experienced in the tracheobronchial tree.

AUTHOR: Banerjee R.; Bellare J.R.; Puniyani R.R.

CORPORATE SOURCE: R. Banerjee, Cardiovascular Research Institute, University

of California, San Francisco, CA 94118-1245, United States.

rban@itsa.ucsf.edu

SOURCE: Biochemical Engineering Journal, (2001) 7/3 (195-200).

Refs: 28

ISSN: 1369-703X CODEN: BEJOFV

PUBLISHER IDENT.: S 1369-703X(00)00124-8

COUNTRY:

Netherlands

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis

027 Biophysics, Bioengineering and Medical

Instrumentation

037 Drug Literature Index

039 Pharmacy

LANGUAGE: English
SUMMARY LANGUAGE: English

A surface active layer consisting mainly of phospholipids lines the human conducting airways. Dysfunction of this layer could play a role in the pathogenesis of chronic obstructive airway diseases like asthma and chronic bronchitis. Replacement therapy with exogenous surfactants is being considered in such conditions. The relationship between surfactants and mucus viscosity would be important for such an application. Respiratory mucus is composed of high molecular weight glycoprotein molecules which form temporary cross-links and entanglements to form a gel-like material. The present paper studies the interaction of three therapeutic surfactants - Exosurf, ALEC and Survanta; the main phospholipids of lung surfactant (1,2-dipalmitoyl phosphatidylcholine (PC), phosphatidylethanolamine (PE) and phosphatidylglycerol (PG)) as well as their binary mixtures (PCPE and PCPG) in a PC: (PE or PG) ratio of 2:3; on the viscosity of mucus gel simulants (MGS - a polymeric gel consisting mainly of gum tragacanth and simulating respiratory mucus). The surfactants were studied with respect to their ability to alter MGS viscosity at shear rates ranging from 0.1498 to 51.2s(-1) in a concentric cylinder viscometer at 37.degree.C. The change in viscosity of the MGS on incubation with surfactant versus shear rate was found be non-Newtonian and to follow a power law model (coefficient of regression R(2) .gtoreq. 0.9). The shear rates experienced by a surfactant mixture, while passing through the tracheobronchial tree, were then calculated by modelling the tracheobronchial tree as cylindrical branching tubes. The equation governing the flow of a power law fluid through a cylindrical pipe was used to determine the shear experienced by a surfactant infusion as it passes through various mucus lined branches of the tracheobronchial tree. The surfactants were then compared based on their ability to alter MGS viscosity at shear rates corresponding to that of large, medium and small bronchi, as calculated by the study. . COPYRGT. 2001 Elsevier Science B.V.

L77 ANSWER 29 OF 32 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2000378607 EMBASE TITLE: Ciliary function. AUTHOR: Van der Baan B.

CORPORATE SOURCE: B. Van der Baan, ENT Department, Univ. Med. Centrum

Utrecht, Vliegheiweg 6, NL-1272 PK Huizen, Netherlands.

vanderbaan@planet.nl

Acta Oto-Rhino-Laryngologica Belgica, (2000) 54/3 SOURCE:

> (293-298). Refs: 5

ISSN: 0001-6497 CODEN: AORLAE

COUNTRY: Belgium

DOCUMENT TYPE: Journal; Conference Article Otorhinolaryngology FILE SEGMENT: 011 Drug Literature Index 037

LANGUAGE: English SUMMARY LANGUAGE: English

Ciliary function. In this article a review is presented of the morphology and function of respiratory cilia and emphasis is placed on the importance of mucociliary clearance as the most important defense mechanism of the upper and lower airways. Physical factors and pharmacological substances which can influence ciliary activity and mucociliary transport are mentioned. Finally, a description is given of changes, mostly reversible, of the mucociliary transport system in infections and IgE-mediated allergy and of the, irreversible changes in congenital diseases like cystic fibrosis and primary ciliary dyskinesia, with some remarks as to the therapeutical consequences of these disturbances.

ANSWER 30 OF 32 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

79121517 EMBASE ACCESSION NUMBER:

DOCUMENT NUMBER: 1979121517

[Bronchial fluidifying agents]. TITLE: LES FLUIDIFIANTS BRONCHIQUES.

AUTHOR: Bonnaud F.; Germouty J.

CORPORATE SOURCE: Serv. Pathol Resp., CHU, 87031 Limoges, France Gazette Medicale de France, (1979) 86/9 (901-908). SOURCE:

CODEN: GAMFA7

COUNTRY: DOCUMENT TYPE:

France Journal

037

FILE SEGMENT: Drug Literature Index

LANGUAGE: French

L77 ANSWER 31 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:167001 BIOSIS PREV200200167001 DOCUMENT NUMBER:

TITLE: Use of dextran and other polysaccharides

to improve mucus clearance.

King, Malcolm (1); Speert, David P. AUTHOR(S):

(1) Edmonton Canada CORPORATE SOURCE:

ASSIGNEE: The University of British Columbia, Vancouver,

Canada; The University of Alberta, Alberta, Canada

PATENT INFORMATION: US 6339075 January 15, 2002

SOURCE: Official Gazette of the United States Patent and Trademark

Office Patents, (Jan. 15, 2002) Vol. 1254, No. 3, pp. No Pagination. http://www.uspto.gov/web/menu/patdata.html.

e-file.

ISSN: 0098-1133.

DOCUMENT TYPE: Patent LANGUAGE: English

This invention relates to the use of polysaccharide such as

dextran to improve mucus clearance. In the present

invention, dextran has been shown to reduce viscoelasticity and

increase mucus clearability of sputum of cystic

fibrosis patients. Dextran also reduced viscoelasticity of healthy dog mucus. The present invention therefore may be

used to improve mucus clearance in cystic

Khare 09/892,636

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fibrosis patients and treat other conditions associated with defect in airway mucus clearance including chronic bronchitis, bronchiectasis and bronchial asthma.

L77 ANSWER 32 OF 32 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:100570 BIOSIS DOCUMENT NUMBER: PREV200000100570

TITLE: Lung delivery of aerosolized dextran.

AUTHOR(S): Finlay, Warren H. (1); Lange, Carlos F.; King, Malcolm;

Speert, David P.

CORPORATE SOURCE: (1) Aerosol Research Laboratory, Department of Mechanical

Engineering, University of Alberta, Edmonton, AB, T6G 2G8

Canada

SOURCE: American Journal of Respiratory and Critical Care Medicine,

(Jan., 2000) Vol. 161, No. 1, pp. 91-97.

ISSN: 1073-449X.

DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

The ability of nebulizers to deliver dextran (nominal molecular mass, 4,000 g/mol) to the lung as an inhaled aerosol is evaluated by in vitro experimental methods and mathematical models. Dextran in isotonic saline was aerosolized by four nebulizer types (Pari LC STAR, Hudson T-Updraft II, Acorn II, and Sonix 2000) at dextran concentrations gtoreq 400 mg/ml and with 2.5- and 4-ml volume fills. Aerosols inhaled during breath simulation were characterized by in-line phase Doppler anemometry, filter collection, osmometry, and gravimetry. Mathematical models were used to estimate amounts of the characterized aerosols depositing in the different regions of lung models, and mathematical models of mucous thickness were then developed to estimate initial concentrations of the depositing dextran in the mucus of each conducting airway generation. Models of three subjects (4 yr old, 8 yr old, and adult) were used. The high viscosity of the dextran solutions tested (up to seven times that of water) negatively impacts nebulization, and results in poor performance with most delivery systems tested. Our results suggest that airway mucosal dextran concentrations associated with efficacy in previous animal and in vitro models are achievable with reasonable delivery times (ltoreq 12 min) with only one of the delivery systems/formulations tested: the Pari LC STAR nebulizer, using a 2.5-ml volume fill and a dextran concentration of 200 mg/ml.

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